UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,221	12/13/2001	Nathan S. Lewis	CIT1300-1	9894

41790 7590 06/14/2006

BUCHANAN INGERSOLL LLP
(INCLUDING BURNS, DOANE, SWECKER & MATHIS)
P.O. BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,221	LEWIS ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 3.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 9-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 9-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 December 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed March 23, 2006 ("Amendment") have been fully considered but they are not persuasive. The Examiner respectfully disagrees that Applicants have through their arguments and reasoning, documentary evidence, and combinations thereof demonstrated that the one with ordinary skill in the art at the time of the invention would know, based on Applicants' disclosure and conventional knowledge at the time, how to adapt any of the very different types of claimed differentially-responsive sensor types (claims 11 and 12) to identify the activity, chemical or physical property, or function of complex biomolecules such as proteins, enzymes, or nucleic acids. Applicants refer to the Drummond et al. article again as evidence of enablement; however, as stated in the Advisory action (February 23, 2006), 'Drummond et al. does not disclose an array of different differentially responsive sensors. The sensor in Drummond et al. is in fact very specific as it comprises a recognition layer for hybridizing with target DNA. See Figures 1-3. Also, it is not clear that a mass-based transducer can be readily substituted for an electrochemical transducer as Drummond et al. states, "Although reliable operation of the QCM in aqueous solution has been a technical challenge, new amplification strategies may overcome this limitation." See first column on page 1193. '

Status of Rejections pending since the Office action of February 23, 2006

2. The rejection of claims 9-16 under 35 U.S.C. 112, first paragraph, is maintained. It is restated below for Applicants' convenience.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for predicting the inhibitory action of alcohols on cytochrome P-450 aniline p-hydroxylation and perhaps some other properties of alcohols or simple organic molecules, such as vapor pressure, does not reasonably provide enablement for predicting or determining the specific activity, chemical or physical property, or function of compounds other than alcohols. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants claim a device that can predict or determine the specific activity, chemical or physical property, or function of an unknown analyte by comparing its signal profile from a sensor array to a collection of sensor array signal profiles from other substances. Claim 16 is unbounded in terms of what the analyte can be and what specific activity, chemical or physical property, or function can be determined or predicted. The last paragraph of claim 16 uses the open term "comprises" and lists a very extensive list of organic functional groups. In the Office action of June 08, 2005 the Examiner asked whether the limitation in the last paragraph of claim 16 means that the primary functionality of the analyte is one of the listed functionalities, or whether, for example, a DNA molecule would be an analyte as contemplated by claim 16. Since Applicants have not commented one way or the other, the examiner assumes that analytes such as those listed in original claims 4-7 are considered to be within the scope of claim 16.

Claim 16 is also unbounded as to the type of sensor array. Claim 11 states that the sensors may change optically, electrically, magnetically, mechanically, physically, or a combination thereof.

The invention of claims 9-16 is of a complex nature as it uses a computer-supported system not to identify or quantitate, but to determine specific activities, chemical or physical properties, or functions of an unlimited scope of analytes including enzymes and nucleic acids with any type of sensor array.

A review of related work in the field shows that others have limited themselves to more modest goals of predicting a particular property on a select type of analyte, such as monitoring sausage fermentation[1], predicting gasoline properties[2], or discriminating chirality with simple gas sensors[3].

The specific activities, chemical or physical properties, or functions of analytes such as antibodies, enzymes, proteins and nucleic acids are rarely predictable. If otherwise, there would be no need for the many hundreds of journal articles on these substances written in dozens of biochemical and chemical journals each year. Old Yellow Enzyme, an arbitrary choice, is illustrative. Although it had been discovered and purified almost 60 years before the time of the invention of the claimed invention and much research had been done on this substance it was only in the few years prior to the invention of the claimed invention that the enzymatic properties and structure-function relations were better understood. Its physiologic role is still unknown. See the Coordinating Editor's comment and the abstract in "Flavoprotein Structure and Mechanism 8 – Structure-function relations for old yellow enzyme" by Karplus et al. The FASEB Journal, vol. 9, December 1995.

Applicant's only example in his disclosure is predicting "the inhibitory action of a series of alcohols on cytrochrome P-450 aniline p-hydroxylation" (described on pages 22-35 of the specification). This involves passing gas phase alcohols over the sensor array to "train" it with alcohols used as standards and to test the sensor array with

---

[1] Ekov et al. « Monitoring sausage fermentation using an electronic nose, » Journal of the Science of Food and Agriculture (1998), 76(4), 525-532.
[2] Litani-Barzlai et al. « Online remote prediction of gasoline properties by combined optical methods, » Analytica Chimica Acta (1997), 339(1-2), 193-199.

unknown alcohols. With only this example as guidance one with ordinary skill in the art would not be able to use Applicant's invention to predict the specific activity, a binding activity, an inhibitory activity, or a modulating activity of an enzyme, let alone predict the secondary, tertiary, or quaternary structures of proteins, or predict the functions of various antibodies or antigens or RNA or DNA sequences, without undue experimentation, if such predictions could be made at all using a sensor array response profile. Should enzymes, proteins, and nucleic acids be also put into the gas phase and passed over the same array of sensors? How is one with ordinary skill in the art to select the right sensor for the unknown analyte of interest and the specific activity, chemical or physical property, or function of the analyte to be predicted? Can crystalline colloidal array sensors and capacitance sensors (claim 12) be used for enzymes and antibodies? Can these sensors be used to determine any specific activity, chemical or physical property, or function of enzymes and antibodies? How is a magnetic sensor array to be used to predict the inhibitory action of alcohols on cytochrome P-450 aniline p-hydroxylation?

---

[3] Bodenh ēfer et al., « Chiral discrimination by Simple Gas-sensors, » Transducers '97, June 16-19, 1997

Thus, the scope of claims 9-16 is too broad because of the almost unlimited scope of the claims in terms of analyte and analyte property, the state of the art and relative skill in the art at the time of invention, the limited guidance and example provided by Applicant's disclosure, the unpredictability of properties of various proteins, enzymes, antibodies, DNA and RNA, and the undue experimentation required to use the analyte screening system.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ballantine, Jr. et al. (Correlation of Surface acoustic Wave Device Coating Response with Solubility Properties and Chemical Structure Using Pattern Recognition," Anal. Chem. 1986, 88, 3058-3066) ("Ballantine").

Addressing claims 16 and 17, Ballantine disclsoes an analyte screening system, comprising

a plurality of different differentially rsponsive sensors (Figuers 1, Table II, and third full paragrpah in the first column on page 3059);

a measuring device, connected to the sensors (Figure 1 and third parpagh in Experimental Section – Analytical System on page 3059);

a computer (third parapagh in Experimental Section – Analytical System on page 3059);

a data storage device in communication with the computer (third parapagh in Experimental Section – Analytical System on page 3059); and

a plurality of signal profiles from a plurality of standard samples of interest, having a known chemical property (solubility of solute vapor in solvent sensor coating - Discussion on page 3064) stored on the ata storage device (Table I, third full parpagh in the first column on page 3059, and third parapagh in Experimental Section – Analytical System on page 3059);

the measuring device detecting a signal from each of the plurality of different differentially responsive seonsors when the sensor array is contacted with the analyte of interest and the computer comprising instruciotns on a ciomputer readable program for causing the computer to assemble the signals from each of the sensors in to a sensor array profile (Experimental Section – Data Collection and Analysis and Experimental Section – Pattern Recognition on page 3061); and

wherein the computer is operative to compare a sensor signal profile to other previously obtained signal profiles of standard samples to identify the chemical property that most closley correlates with the sensor signal profile, wherein the correlation of the sensor array signal profile, wherein the correlation of the sensor signal profiles to the previously obtained signal profiles is predictive of a chemical property (Experimental Section – Pattern Recognition on page 3061 and Results – Pattern Recognition on page 3083).

Note that the examainer has broadly construed "sensor array." Since Ballantine does disclose 12 sensors exposed to the same samples and whose respones are combined, a sensor array is disclosed. Furthermore, Ballantine discloses that ten sensors account for 99% of the data variance (first parpagh of Results – Pattern Recognition on page 3083), so it would have been obvious to one with ordinary skill in the art at the time of the invention that have the sensors arranged in an array because this will give a more accurate identication of the chemical property than if just one of the sensors is used.

Ballantine does not mention having the plurality of signal profiles from a plurality of standard samples not include an analyte of interest. However, Ballantine uses several pattern recognition techniques to construct discriminate functions for classifying the samples as to their strengths as a hydrogen bond donor or hydrogen bond accepter (Experimental – Pattern Recognition on page 3061 and Discussion on page 3064 – 3066). It would have been obvious to one with ordinary skill in the art at the time of the invention to have the plurality of signal profiles from a plurality of standard samples not include an analyte of interest, that is, to use the discriminant functions to identify the chemical property of samples other than the standards or training compounds, because Ballantine states, " ... it is clear that the combination of multiple sensor arrays of coated SAW devices and appropriate pattern recognition software will provide a sensor system that can be selective as well as sensitive for a *broad spectrum of compounds.*[emphasis added]" See Conclusions on page 3066..

For the limitation of the analyte comprising or consisting essentially of at least an alkane, hydrocarbon, alcohol, or ketone, etc., note that several of the standards used by Ballantine to "train" the sensors comprise or consist essentially of at least an alkane, hydrocarbon, alcohol, or ketone (see Table I), thus one with ordinary skill in the art at the time of the invention would use the sensor on samples having at least one or more or these types of compounds as analytes; that is, on at least analytes similar to the standards.

Addressing claim 11, for the additional limitation of this claim see the first paragraph after the abstract, which discloses that surface acoustic wave devices are mass-sensitive detectors (change physically).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753